PERGAMON

Neuropsychologia 41 (2003) 245–251

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Competition among multiple memory systems: converging evidence from animal and human brain studies

Russell A. Poldrack [a,*], Mark G. Packard [b]

[a] *Department of Psychology and Brain Research Institute, Franz Hall, University of California at Los Angeles, P.O. Box 951563, Los Angeles, CA 90095-1563, USA*

[b] *Department of Psychology, Texas A & M University, College Station, TX, USA*

Abstract

Research of the neurobiological bases of learning and memory suggest that these processes are not unitary in nature, but rather that relatively independent neural systems appear to mediate different types of memory. Neurobiological studies, for instance, have identified separable cognitive or "declarative" and stimulus–response "habit" memory systems that rely upon the medial temporal lobe (e.g. hippocampus) and basal ganglia (e.g. caudate–putamen), respectively. Evidence indicates that multiple memory systems are activated simultaneously and in parallel in various learning tasks, and recent findings suggest that these systems may interact. One form of interaction between medial temporal lobe and basal ganglia memory systems appears competitive in nature, and has been revealed in non-human animal studies in which damage to a given memory system results in enhanced learning. Recent human neuroimaging research has also provided evidence in favor of competition between memory systems. Thus, converging evidence across species supports the hypothesis of interactive multiple memory systems in the mammalian brain. Potential neurobiological mechanisms mediating such interactions include direct anatomical projections between the medial temporal lobe and basal ganglia, indirect neuromodulatory influences of other brain structures (e.g. basolateral amygdala) and activity of neocortical brain regions involved in top–down response selection.

Keywords: Multiple memory systems; Brain studies; Animals and humans; Hippocampus; Basal ganglia; Striatum; Medial temporal lobe

1. Introduction

Studies of memory organization in non-human animals and humans have led to a consensus that memory is not a monolithic faculty, but rather is supported by multiple brain systems that differ in terms of the types of memory they mediate. The multiple memory systems hypothesis was originally derived in large part from evidence of a pattern of impaired and spared learning abilities following damage to the mammalian hippocampal system, and several dual-memory theories outlining the psychological operating characteristics of hippocampus-dependent and non-hippocampus-dependent memory have been proposed (e.g. [4,10,23,27,28,47,48]). According to one hypothesis, the hippocampus is an anatomical component of a memory system supporting "declarative" memory, characterized by flexibly accessible, relational memory for past events and facts (e.g. [3,4]). In contrast, memories underlying other learned behaviors (e.g. acquisition of stimulus–response habits, and some forms of Pavlovian conditioning) do not appear to rely crucially upon the hippocampus and other structures of the medial temporal lobe, and may collectively be termed "non-declarative" or procedural memory (e.g. [3,47]).

The existence of multiple memory systems can in part be suggested on the basis of single dissociations (e.g. damage to the hippocampal system impairs acquisition of task A, but not task B). However, there are several reasons why the hypothesis of functional independence between memory systems should be offered cautiously when based on *single* dissociations (for reviews on the use of dissociation methodology see [43,51]). In experimental animals, compelling evidence for the existence of multiple memory systems is provided by studies demonstrating a *double* dissociation following irreversible (e.g. [15,21,22,32,33]) and reversible [12,34] lesion damage to different brain structures, including the hippocampus and caudate–putamen (i.e. dorsal striatum). Additional research in non-human animals has employed post-training intra-cerebral drug infusions to demonstrate a

* Corresponding author.
E-mail address: poldrack@ucla.edu (R.A. Poldrack).

0028-3932/02/$ – see front matter © 2002 Elsevier Science Ltd. All rights reserved.
PII: S0028-3932(02)00157-4

double dissociation between the mnemonic functions of the hippocampus and caudate–putamen [29,35,37].

In humans, double dissociations in task acquisition have been observed between patients with amnesia due to medial temporal lobe damage (who exhibit impaired recognition memory but spared perceptual priming) and patients with lesions to the occipital cortex (who show the opposite pattern) [8,14]. Other double dissociations are evident across studies; e.g. amnesic patients are impaired at recognition memory but exhibit normal motor skill learning (e.g. [49]) whereas patients with Parkinson's (PD) and Huntington's diseases (HD) show the opposite pattern (e.g. [9]). Taken together, the converging evidence from animal and human studies indicates differential roles of the hippocampal system and cortico-striatal systems in memory and suggests that declarative and non-declarative memory systems can, at least in some cases, act independently of one another to support learned behavior.

Despite this apparent independence, other evidence has arisen indicating that multiple memory systems in the mammalian brain may interact with one another. Previous studies of interactions between memory systems have focused primarily on cases in which declarative and non-declarative memory may interact cooperatively, that is, in learning situation in which more than one system can provide a solution. In motor sequence learning, subjects can use either declarative or procedural memory to learn the task [54], and using both systems in a cooperative fashion may optimize learning in some cases. In other cases, subjects may attribute the increased fluency of task processing (putatively reflecting non-declarative memory processes) to various conscious effects of experience [52,53].

Evidence has also arisen suggesting that memory systems may sometimes interact competitively as well. Sherry and Schacter [44] offered an early hypothesis on the potential existence of interference or competition between multiple memory systems. These authors suggested that the presence of "functional incompatibility", in which an existing memory system is unable to provide an adequate solution in a situation involving novel information or task demands, may have driven natural selection processes that ultimately resulted in the evolution of multiple memory systems. In this brief review, we outline converging evidence, arising first from animal studies and more recently from human neuroimaging studies, indicating that memory mechanisms in the medial temporal lobe (e.g. hippocampus) and basal ganglia (e.g. caudate–putamen/dorsal striatum) may compete with one another during some learning situations. These findings suggest an expansion of the multiple memory systems hypothesis, in which memory systems are not viewed solely as independent learning mechanisms, but rather operate as part of a dynamic system with the goal of optimizing behavior based on experience. After reviewing these findings, we explore a number of possible mechanisms for these interactions, and discuss the adaptive utility of interactions between memory systems.

2. Non-human animal studies

As noted above, several examples exist of double dissociations in task acquisition following lesion damage to the hippocampal system and caudate–putamen, and post-training intra-cerebral drug infusions into these two structures. In considering the nature of potential system interactions, the use of a learning task in which both systems can provide a solution reveals an interesting temporal aspect of multiple memory system use. Specifically, early learning is mediated by the hippocampal system, and with extended training, the dorsal striatal system comes to guide learned behavior. This "timeline" of multiple memory system use has been demonstrated [34] using a plus-maze task in which rats obtain food in a goal box (west) by approaching this maze arm from the same start box on each trial (south). Following training rats are given a probe trial in which they are placed in the start box opposite to that used during training (north). On the probe trial, rats that enter the west arm (i.e. the spatial location where food was located during training) are designated "place" learners, and rats that enter the east arm (i.e. make the same body turn response that had been reinforced during training) are designated "response" learners. On an initial probe trial given early in training, rats receiving intra-caudate or intra-hippocampal infusions of saline are predominantly place learners. Rats receiving intra-caudate infusions of the local anesthetic lidocaine (in order to produce neural inactivation) are also place learners on this initial probe trial, whereas intra-hippocampal infusions of lidocaine block the expression of place learning. With extended training in this plus-maze task, administration of a second probe trial reveals that saline-infused rats switch from the use of place learning to response learning tendency. On this second probe trial rats receiving intra-hippocampal lidocaine are also response learners. In contrast, rats receiving intra-caudate lidocaine prior to the second probe trial exhibit place learning, demonstrating a blockade of the expression of response learning. This finding also indicates that when the shift from the use of hippocampus-dependent place to caudate-dependent response learning occurs, the place representation can be "unmasked" by blockade of the response learning system.

Taken together, these findings suggest that in tasks in which these two systems can each provide an adequate learned solution, simultaneous activation of hippocampal and caudate memory systems occurs (for another example of this principle, see [22]). Moreover, it appears that in tasks in which these two memory systems may interact cooperatively, early learning is mediated by the hippocampal system, and with extended training the dorsal striatum comes to guide learned behavior. Interestingly, the time course of this shift from the use of "cognitive" to "habit" memory can be influenced by intra-cerebral infusions of the amino acid neurotransmitter glutamate [29]. Specifically, rats receiving post-training intra-hippocampal infusions glutamate during early time points in plus-maze training subsequently display

place learning on *both* an early and late probe trial. This finding suggests that infusion of glutamate into the hippocampus strengthens a place learning representation, effectively blocking the shift to response learning that normally occurs with extended training. In contrast, rats given post-training glutamate infusions into the caudate–putamen subsequently display response learning on *both* the early and late probe trials, suggesting that infusion of glutamate into the caudate–putamen accelerates the shift to response learning that occurs in control rats only following extended training.

In contrast to learning tasks that may be acquired by more than one memory system, in other situations an interfering or competitive interaction between multiple memory systems may occur. Competitive interference between different memory systems may be revealed in studies in which pre-training lesions of a given system result in *enhanced* acquisition of a task relative to brain-intact animals. The enhancing effect of hippocampal system lesions on acquisition of caudate-dependent two-way active avoidance behavior, for instance, has been hypothesized to result from the removal of spatial information processing that would interfere with the task requirement of *returning* to a spatial location in which electrical shock has recently been administered (e.g. [27]). In addition, in a caudate-dependent win-stay radial maze task in which rats are required to visit each of four illuminated maze arms twice within a daily training session, hippocampal spatial memory processes provides the rat with information concerning those maze arms in which food has *already* been retrieved, and may interfere with the task requirement of *revisiting* maze arms in which food was recently removed. Consistent with this hypothesis, pre-training lesions of the hippocampal system facilitate acquisition of this caudate-dependent task [21,32]. Similarly, lesions of the caudate–putamen have been reported to facilitate acquisition of a spatial Y-maze discrimination task [24], perhaps by disrupting the use of a potentially interfering response strategy. Finally, whereas pre-training lesions may act to eliminate competition between multiple memory systems by removing "on-line" processing during task performance, recent evidence indicates that post-training reversible inactivation of the hippocampus can also enhance caudate-dependent response learning [42]. This finding raises the interesting possibility that competitive interference between multiple memory systems may in part occur during the memory consolidation period.

3. Human neuroimaging

Evidence of competition between the medial temporal lobe and caudate nucleus in humans was provided by a recent study of probabilistic classification learning [40]. In this task (known as the "weather prediction task"), subjects are presented on every trial with a set of cards depicting abstract shapes, and are asked to decide whether that set of cards predicts one of two outcomes ("rain" (R) or "sunshine" (S)). Following each decision subjects are given feedback, and the subject acquires the classification based on this feedback. The feedback is probabilistic, such that different outcomes will be given as feedback for the same set of cards on different trials (with a given probability). Therefore, this task may be acquired incrementally in a S–R habit manner. Neuropsychological investigation of this task has demonstrated that patients with Parkinson's and Huntington's diseases are impaired at learning the classification, whereas patients with MTL amnesia learn normally early in training but are impaired later in training relative to controls [16,17]. These findings led to the suggestion that learning was based primarily upon neostriatal systems, but that the MTL became important later in training as well.

During fMRI acquisition, subjects received alternating blocks of weather prediction trials and baseline trials. On baseline trials, subjects decided how many cards were presented, equating the essential perceptual and motor demands of the weather prediction task. Comparison with the baseline task showed a large set of brain regions that were more active during weather prediction, including bilateral prefrontal and parietal regions. Consistent with the impairments of PD and HD patients on the task, activity was observed in the caudate nucleus, confirming the importance of the basal ganglia for this task.

An additional analysis examined whether particular brain regions were significantly less active (or "deactivated") during weather prediction compared to baseline. Such deactivations often go unreported in brain imaging studies, and when they are reported there is a consistent set of regions that appear to be deactivated across studies, including medial prefrontal and medial parietal cortex [45]. In the weather prediction task, these brain regions were deactivated, but in addition to those regions, deactivation was also found in the medial temporal lobe. Further examination of the individual subject data showed that six of eight subjects had deactivation in the left hippocampus, five in the right hippocampus, and two had additional deactivation in the medial temporal (parahippocampal/perirhinal) cortex. Analysis of the time course of this deactivation showed that it become more pronounced over the first 48 trials, and then appeared to dissipate towards 96 trials (the length of the study).

A subsequent set of studies [38] examined whether deactivation extended out to 144 training trials on the weather prediction task using a blocked design similar to the initial study. Interestingly, deactivation was maintained through 144 trials with no sign of abatement, suggesting that the MTL does not become engaged later in training. Note that 144 trials is well beyond the point at which MTL amnesics have become impaired relative to controls. This study also examined whether the deactivation was specific to a feedback-driven version of the task, by comparing performance on that version to performance of another group of subjects on a paired-associate learning version of the task. In this version, subjects were presented with the same stimuli and probabilistic outcomes, but they were simply asked to

learn the relationships and did not respond with classification judgments on each trial. Although these subjects learned the classification as accurately as those subjects in the standard feedback-driven version of the task, there was a significantly greater MTL deactivation in the feedback-based version of the task, demonstrating that the deactivation is driven by particular task demands.

Another question raised by the finding of MTL deactivation was whether there were other brain regions whose activity was negatively correlated with MTL activity, which would suggest a negative functional relationship. In order to examine this question, the level of signal from the MTL was extracted for each subject and re-entered into a correlational analysis with all other voxels in the brain [38]. This analysis found that activity in the caudate nucleus was negatively correlated with activity in the MTL across subjects, providing evidence that the concurrent striatal activation and MTL deactivation was not coincidental. However, because this is a correlational analysis it cannot demonstrate that this relationship is causal, or that some other brain region does not drive it. Furthermore, the caudate nucleus and MTL showed a reciprocal relationship in activity across trials, with the MTL activated and caudate deactivated early in training, but the MTL becoming deactivated and the caudate becoming activated as learning progressed. Thus, both across subjects and across time there was a negative relation between activity in the MTL and caudate nucleus, consistent with competition between these regions.

A number of other neuroimaging results appear to be consistent with competition between the MTL and basal ganglia. First, beyond the studies of cognitive skill learning described above, other studies of both motor skill learning [11] and perceptual skill learning [39] found increasing activation in the striatum (putamen and caudate, respectively) which was accompanied by increasing deactivation of the MTL. Second, PET imaging during performance of a planning task (the Tower of Toronto) showed that normal subjects exhibited increasing striatal activity and decreasing MTL activity as task difficulty increased, whereas patients with Parkinson's disease showed neither of these changes even though their level of performance was equivalent to the controls [5]. Finally, a recent report using fMRI [25] replicated the findings of striatal activation and MTL deactivation in normal subjects during the weather prediction classification task, and further showed that both of these responses were attenuated in patients with Parkinson's disease. Together these results provide increasing evidence that in some learning situations, there is a negative relationship in activity between the striatum and MTL.

It is clear from previous studies and from subjects' reported experience on probabilistic classification tasks that normal subjects are fully able to explicitly report on their experiences during training on the task. This implies that deactivation of the MTL is not associated with wholesale disruption of episodic memory encoding processes. It is instead more likely that this deactivation reflects the modulation of episodic memory retrieval, or of its contribution to task performance.

It is important to note that all of these imaging results come with an important caveat. Specifically, the synaptic correlates of medial temporal lobe deactivation remain to be characterized, and the functional significance of neural deactivation is not understood. A correlation between fMRI signals and neural activity (specifically, local field potentials rather than spike activity) has recently been demonstrated [19], however, it is unclear how this finding can be extended to deactivations. In addition, it is unclear to what degree results from the primary visual cortex can be extended to the hippocampus and related structures in the medial temporal lobe, given their unique neural architectures. Nonetheless, there is reason to believe that the deactivations observed in the MTL during classification learning are directly related to the engagement of particular striatal learning mechanisms. In particular, as noted above the use of instructions designed to encourage the engagement of declarative memory resulted in a decrease in striatal activation and concomitant abatement of MTL deactivation [38].

4. Potential neurobiological mechanisms mediating multiple memory system interactions

Whereas extensive evidence indicates that mammalian memory processes are organized in multiple brain systems that include the hippocampus and caudate nucleus, little is currently known concerning the neurobiological mechanisms mediating interactions between neostriatal and MTL-based memory systems. Possible mechanisms include direct anatomical projections between these systems, indirect modulatory influences of other brain structures, and influences at the level of response-selection processes.

5. Direct anatomical influences

The most obvious possible mechanism for mediating competition between multiple memory systems is direct anatomical connections between the MTL and striatum, and there is evidence for such connections. Although most efferents from the medial temporal lobe appear to target the ventral striatum (particularly the nucleus accumbens) there is evidence from tract-tracing methods for direct projections from the entorhinal cortex to the dorsal striatum in rats [46]. Using neurophysiological techniques in rats, Finch and colleagues [6,7] have demonstrated that stimulation of both entorhinal and hippocampal (subiculum/CA1) neurons results in responses in both the caudate–putamen and ventral striatum. The majority of cauduate-putamen responses to entorhinal cortex stimulation were inhibitory [7], consistent with a negative influence between these structures.

Evidence for efferent connections from the neostriatum to MTL is somewhat less direct than the converse. The

strongest evidence comes from studies in the cat demonstrating that caudate nucleus stimulation effectively reduces the occurrence of hippocampal spikes resulting from penicillin administration to the hippocampus [18,41]. In particular, caudate stimulation appears to induce theta rhythm in the hippocampus. This is particularly interesting in the present context, given previous findings that theta rhythm in rats is associated with decreased glycogen phosphorylase activity (a marker of metabolic activity) in the hippocampus [50]. It appears that the effects of caudate stimulation on hippocampal spike activity are mediated by cholinergic mechanisms, as administration of atropine or septal lesions both attenuate the ability of caudate stimulation to reduce hippocampal spike activity [18].

6. Indirect modulatory influences

It is also possible that mnemonic interactions between striatum and MTL are mediated by the activity of other brain structure(s). One such potential mechanism would involve the activity of a neuromodulatory system that has differential effects in the two structures. Consistent with this possibility, recent evidence suggests that the basolateral amygdala exerts a memory modulatory influence on the distinct memory processes mediated by the hippocampus and dorsal striatum [31,36]. Specifically, post-training intra-basolateral amygdala infusions of amphetamine enhance memory in both hippocampus-dependent and striatal-dependent learning tasks. This memory modulatory influence of the basolateral amygdala on multiple memory systems appears to involve activation of efferent amygdala pathways. Moreover, the modulatory influence of the basolateral amygdala on the relative use of hippocampal and caudate memory processes may be related to the well-established role of the amygdala in emotional arousal [30]. For example, in a plus-maze task in which both hippocampus-dependent place learning and caudate-dependent response learning can provide a task solution, pre-training peripheral and intra-basolateral amygdala infusion of anxiogenic drugs results in the predominant use of response learning (Packard and Wingard, unpublished data).

7. Response-level interactions

At this early stage of investigation of the interaction among multiple memory systems, it seems parsimonious to attribute the observed interactions between striatum and MTL to direct or indirect neural connections between the two structures. However, it is also possible that the interaction is driven by feedback connections from structures involved in response selection or production. This effect could be conceptualized in terms of the top–down attentional modulation effects that have been observed both in animals using neurophysiology [26] and in humans using neuroimaging [13]. That is, some strategic process would exert a top–down signal that would modulate the degree of activity in the various systems whose outputs are relevant to performing the current task. Such a strategic process would likely be implemented within the “cognitive” fronto-striatal circuit involving dorsolateral prefrontal cortex and head of caudate [1].

8. Conclusions

Extensive evidence indicates that components of the MTL (e.g. hippocampus) and basal ganglia (i.e. dorsal striatum) can function as independent memory systems in some learning situations, and the findings reviewed here clearly suggest that multiple memory systems may also interact with each other. Whereas early evidence for multiple memory system interactions was provided in experimental animal research, such evidence has also recently arisen in studies of human brain function, spurred by the development of novel neuroimaging techniques such as fMRI. Many questions remain regarding the nature of these memory system interactions. For non-human animal studies, main outstanding questions center on the neurophysiological and neuropharmacological bases of the interactions that have been observed. For human neuroimaging studies, one of the main outstanding questions regards the neurobiological nature of the deactivations that have been consistently observed in the context of learning tasks that engage the striatum. Another outstanding question concerns the decomposition of complex tasks such as the weather prediction task; in order to determine which task components are responsible for the negatively related activation observed in MTL and striatum.

At present our understanding of how various physiological, environmental, and/or training parameters influence the interaction among multiple memory systems is poorly understood, and such questions represent a fertile area for future investigation. It seems unlikely that a complete understanding of the dynamics underlying learning and memory processes can be reached without elucidation of the factors that shape interactions among multiple memory systems, including those that may occur during development (e.g. [2,20]). Investigators involved in developing computational models of memory also need to incorporate the notion of system interactions, at least to the extent that such models seek to explain learning and memory processes as they are computed by the intact mammalian brain.

References

[1] Alexander GE, DeLong MR, Strick PL. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annual Review of Neuroscience 1986;9:357–81.

[2] Bachevalier J, Mishkin M. An early and a late developing system for learning and retention in infant monkeys. Behavioral Neuroscience 1984;98:770–8.
[3] Cohen NJ, Eichenbaum HE. Memory, amnesia, and the hippocampal system. Cambridge (MA): MIT Press; 1993.
[4] Cohen NJ, Squire LR. Preserved learning and retention of pattern-analyzing skill in amnesia: dissociation of knowing how and knowing that. Science 1980;210(4466):207–10.
[5] Dagher A, Owen AM, Boecker H, Brooks DJ. The role of the striatum and hippocampus in planning: a PET activation study in Parkinson's disease. Brain 2001;124(Part 5):1020–32.
[6] Finch DM. Neurophysiology of converging synaptic inputs from the rat prefrontal cortex, amygdala, midline thalamus, and hippocampal formation onto single neurons of the caudate/putamen and nucleus accumbens. Hippocampus 1996;6(5):495–512.
[7] Finch DM, Gigg J, Tan AM, Kosoyan OP. Neurophysiology and neuropharmacology of projections from entorhinal cortex to striatum in the rat. Brain Research 1995;670(2):233–47.
[8] Gabrieli JDE, Fleischman DA, Keane MA, Reminger SL, Morrell F. Double dissociation between memory systems underlying explicit and implicit memory in the human brain. Psychological Science 1995;6:76–82.
[9] Heindel WC, Salmon DP, Shults CW, Wallicke PA, Butters N. Neuropsychological evidence for multiple implicit memory systems: a comparison of Alzheimer's, Huntington's and Parkinson's disease patients. Journal of Neuroscience 1989;9:582–7.
[10] Hirsh R. The hippocampus and contextual retrieval of information from memory: a theory. Behavioral Biology 1974;12:421–44.
[11] Jenkins IH, Brooks DJ, Nixon PD, Frackowiak RSJ, Passinghem RE. Motor sequence learning: a study with positron emission tomography. Journal of Neuroscience 1994;14(6):3775–90.
[12] Kantak KM, Green-Jordan K, Valencia E, Kremin T, Eichenbaum HB. Cognitive task performance after lidocaine-induced inactivation of different sites within the basolateral amygdala and dorsal striatum. Behavioral Neuroscience 2001;115(3):589–601.
[13] Kastner S, De Weerd P, Desimone R, Ungerleider LG. Mechanisms of directed attention in the human extrastriate cortex as revealed by functional MRI. Science 1998;282(5386):108–11.
[14] Keane M, Gabrieli JDE, Mapstone HC, Johnson KA, Corkin S. Double dissociation of memory capacities after bilateral occipital-lobe or medial temporal-lobe lesions. Brain 1995;118:1129–48.
[15] Kesner RP, Bolland BL, Dakis M. Memory for spatial locations, motor responses and objects: triple dissociation among the hippocampus, caudate nucleus, and extrastriate visual cortex. Experimental Brain Research 1993;93(3):462–70.
[16] Knowlton B, Squire LR, Gluck MA. Probabilistic classification in amnesia. Learning and Memory 1994;1:106–20.
[17] Knowlton BJ, Mangels JA, Squire LR. A neostriatal habit learning system in humans. Science 1996;273:1399–402.
[18] La Grutta V, Sabatino M. Focal hippocampal epilepsy: effect of caudate stimulation. Experimental Neurology 1988;99(1):38–49.
[19] Logothetis NK, Pauls J, Augath M, Trinath T, Oeltermann A. Neurophysiological investigation of the basis of the fMRI signal. Nature 2001;412(6843):150–7.
[20] Mahut, H, Moss, M. Consolidation of memory: the hippocampus revisited. In: Squire, LR, Butters N, editors. Neuropsychology of memory. New York: Guilford; 1984. p. 297–315.
[21] McDonald RJ, White NM. A triple dissociation of memory systems: hippocampus, amygdala, and dorsal striatum. Behavioral Neuroscience 1993;107(1):3–22.
[22] McDonald RJ, White NM. Parallel information processing in the water maze: evidence for independent memory systems involving dorsal striatum and hippocampus. Behavioral Neural Biology 1994;61(3):260–70.
[23] Mishkin M, Malamut B, Bachevalier J. Memory and habits: some implications for the analysis of learning and retention. In: Squire LR, Butters N, editors. Neuropsychology of memory. New York: Guilford; 1984. p. 287–96.
[24] Mitchell JA, Hall G. Caudate–putamen lesions in the rat may impair or potentiate maze learning depending upon availability of stimulus cues and relevance of response cues. Quarterly Journal of Experimental Psychology B 1988;40(3):243–58.
[25] Moody TD, Bookheimer SY, Vanek Z, Knowlton BJ. An implicit learning task activates medial temporal lobe in patients with Parkinson's disease, submitted for publication.
[26] Moran J, Desimone R. Selective attention gates visual processing in the extrastriate cortex. Science 1985;229(4715):782–4.
[27] O'Keefe, J, Nadel, L. The hippocampus as a cognitive map. Oxford: Oxford University Press; 1978.
[28] Olton DS, Becker JT, Handelmann GE. Hippocampus space and memory. Behavioral and Brain Sciences 1979;2:313–65.
[29] Packard MG. Glutamate infused posttraining into the hippocampus or caudate–putamen differentially strengthens place and response learning. Proceedings of the National Academy of Sciences of the United States of America 1999;96(22):12881–6.
[30] Packard MG, Cahill L. Affective modulation of multiple memory systems. Current Opinion of Neurobiology 2001;11(6):752–6.
[31] Packard MG, Cahill L, Mcgaugh JL. Amygdala modulation of hippocampal-dependent and caudate nucleus-dependent memory processes. Proceedings of the National Academy of Sciences of the United States of America 1994;91:8477–81.
[32] Packard MG, Hirsh R, White NM. Differential effects of fornix and caudate nucleus lesions on two radial maze tasks: evidence for multiple memory systems. Journal of Neuroscience 1989;9(5):1465–72.
[33] Packard MG, McGaugh JL. Double dissociation of fornix and caudate nucleus lesions on acquisition of two water maze tasks: further evidence for multiple memory systems. Behavioral Neuroscience 1992;106(3):439–46.
[34] Packard MG, McGaugh JL. Inactivation of hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning. Neurobiology of Learning and Memory 1996;65(1):65–72.
[35] Packard MG, Teather LA. Double dissociation of hippocampal and dorsal-striatal memory systems by posttraining intracerebral injections of 2-amino-5-phosphonopentanoic acid. Behavioral Neuroscience 1997;111(3):543–51.
[36] Packard MG, Teather LA. Amygdala modulation of multiple memory systems: hippocampus and caudate–putamen. Neurobiology of Learning and Memory 1998;69(2):163–203.
[37] Packard MG, White NM. Dissociation of hippocampus and caudate nucleus memory systems by posttraining intracerebral injection of dopamine agonists. Behavioral Neuroscience 1991;105(2):295–306.
[38] Poldrack RA, Clark J, Paré-Blagoev J, Shohamy D, Creso Moyano J, Myers C, et al. Interactive memory systems in the human brain. Nature 2001;414:546–50.
[39] Poldrack RA, Gabrieli JD. Characterizing the neural mechanisms of skill learning and repetition priming: evidence from mirror reading. Brain 2001;124(Part 1):67–82.
[40] Poldrack RA, Prabakharan V, Seger C, Gabrieli JDE. Striatal activation during cognitive skill learning. Neuropsychology 1999;13:564–74.
[41] Sabatino M, Ferraro G, Liberti G, Vella N, La Grutta V. Striatal and septal influence on hippocampal theta and spikes in the cat. Neuroscience Letters 1985;61(12):55–9.
[42] Schroeder JA, Wingard J, Packard MG. Post-training reversible inactivation of the dorsal hippocampus reveals interference between multiple memory systems. Hippocampus 2002;12:280–4.
[43] Shallice, T. From neuropsychology to mental structure. New York: Cambridge University Press; 1988.
[44] Sherry DF, Schacter DL. The evolution of multiple memory systems. Psychological Review 1987;94(4):439–54.

[45] Shulman GL, Fiez JA, Corbetta M, Buckner RL, Miezin FM, Raichle ME, et al. Common blood flow changes across visual tasks. II. Decreases in cerebral cortex. Journal of Cognitive Neuroscience 1997;9:648–63.
[46] Sorensen KE, Witter MP. Entorhinal efferents reach the caudato-putamen. Neuroscience Letters 1983;35(3):259–64.
[47] Squire LR. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. Psychological Review 1992;99(2):195–231.
[48] Sutherland RJ, Rudy JW. Configural association theory: the role of the hippocampal formation in learning, memory, and amnesia. Psychobiology 1989;17:129–44.
[49] Tranel D, Damasio AR, Damasio H, Brandt JP. Sensorimotor skill learning in amnesia: additional evidence for the neural basis of nondeclarative memory. Learning and Memory 1994;1(3):165–79.
[50] Uecker A, Barnes CA, McNaughton BL, Reiman EM. Hippocampal glycogen metabolism, EEG, and behavior. Behavioral Neuroscience 1997;111(2s):283–91.
[51] Weiskrantz L. Some traps and pontifications. In: Weiskrantz L, editor. Analysis of behavioral change. New York: Harper & Row; 1968. p. 415–29.
[52] Whittlesea BW, Williams LD. The source of feelings of familiarity: the discrepancy-attribution hypothesis. Journal of Experimental Psychology: Learning Memory and Cognition 2000;26(3):547–65.
[53] Whittlesea BWA. Illusions of familiarity. Journal of Experimental Psychology: Learning Memory and Cognition 1993;19:1235.
[54] Willingham DB. A neuropsychological theory of motor skill learning. Psychology Review 1998;105(3):558–84.